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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/541,752	03/31/2000	Zeren Gao	98-60C1	3712

7590 10/02/2003

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	LS

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/541,752	GAO ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Part III: Detailed Office Action

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 33, 34 and 36 remain rejected under 35 U.S.C. 102(e) as being anticipated by Ferrara et al., U.S. Patent Number 6,391,311 B1, issued 5/21/02.

Ferrara et al. teach a protein they designate VEGF-E, which is 100% identical at residues 235-345 to SEQ ID NO: 2 of this application. Antibodies, including monoclonal antibodies and antibodies linked to reporter molecules, are taught at columns 23-26. As the antibodies of Ferrara et al. would include antibodies binding to the recited portion of SEQ ID NO: 2, the disclosure of Ferrara et al. anticipates the claimed invention.

Applicants have traversed this rejection on the basis that Ferrara does not specifically suggest using residues 235-345 of SEQ ID NO: 2 as an immunogen, and that the teachings of Ferrara would not necessarily lead to the claimed antibodies. This argument has been fully considered but is not deemed persuasive because Ferrara specifically teaches the use of fragments of VEGF-E for the production of antibodies at column 16, lines 33-37. Applicants argue that Ferrara does not teach or suggest the use, as an immunogen, of a polypeptide consisting of residues 235-345 of SEQ ID NO: 2 or a peptide fragment thereof. This argument has been fully considered but is not deemed persuasive because, while Ferrara does not teach specifically using as an immunogen the protein of residues 245-345, neither does the instant specification: Claim 33 finds basis in originally filed claim 33, which was drawn to "an antibody that binds to an epitope of a polypeptide according to claim 3". Originally filed claim 3 was drawn to a large number of species, only one of which (x=0, y=0,

z=1 and is 100% identical, as opposed to 'greater than 90%') is the peptide of 245-345 of SEQ ID NO: 2. At page 54 of the specification, where production of antibodies is discussed, there is mention of using short peptides to make antibodies (similar to the disclosure of Ferrara et al.), but no specific disclosure of using a peptide consisting of residues 245-356 as an immunogen. Therefore, there is no disclosure in the specification of actually using a peptide of residues 245-345 as an immunogen, and applicants arguments that using such a peptide would result in obtaining antibodies different from those taught by Ferrara et al. is not persuasive.

Applicants cite Li et al., as teaching that the conformation of full-length PDGF-C, which is the same as applicants zvegf3, blocks the active region of the molecule. This argument has been fully considered but is not deemed persuasive because the claims are drawn to antibodies that bind *anywhere* in the region of amino acids 245-345. There is no limitation as to blocking the active region of the molecule, and the Li paper does not address the issue of being able to make antibodies to any/all portions of the region. Further, applicants quotation of the Li paper is taken out of context, and is part of a discussion of proteolytic processing of the protein in which the N-terminal CUB domain is removed; it neither states nor implies anything about the likelihood of raising antibodies to the C-terminal portion of the protein. In fact, at the cited paragraph, Li et al. state that "removal of the N-terminal (CUB) domain may be unlikely to induce a new receptor-binding epitope." The Examiner makes the Li paper of record herein. It remains that given Ferrara's teaching, that one would obtain antibodies within the metes and bounds of the claims. The declarations are discussed below.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 35 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al., U.S. Patent Number 6,391,311 in view of U.S. Patent Number 4,946,778 (Ladder et al.) for reasons of record in the previous Office Action. Applicants arguments are not persuasive for reasons cited above, and the declaration evidence is fully considered below.

Consideration of Declarations:

The declaration by Dr. Clegg under 37 CFR 1.132 filed 7/11/03 is insufficient to overcome the art rejections as set forth in the last Office action because: The declaration is merely an opinion declaration, and does not present any facts or evidence regarding the predictability of obtaining antibodies to the claimed region of the protein when using fragments of the protein, as taught by Ferrara et al. Further, the limitations discussed in paragraph 7 of the declaration are not pertinent to the rejection, as the rejection is not limited to the teachings of the claims of the Ferrara patent.

The declaration by Mr. Pelto under 37 CFR 1.132 filed 7/11/03 is insufficient to overcome the art rejections as set forth in the last Office action because:

Mr. Pelto states that he performed an experiment to test the ability of antisera raised against a full-length zvefg3 protein to recognize different forms of zvegf3. At paragraph 5, Mr. Pelto states that a Western blot was carried out in which binding of polyclonal antisera to various proteins was assessed. He concludes that the antisera did not recognize any of the samples of isolated zvegf3 growth factor domain.

The experiment described by Mr. Pelto is not sufficient to address the art rejection over Ferrara et al., as Ferrara's disclosure is not limited to making antibodies to the full-length protein (or even the protein claimed by Ferrara et al.), but rather discloses antibodies raised to *fragments* of the full-length protein; if the entire protein were fragment for the production of antibodies, the claimed antibodies would surely be obtained. Further, as Li et al. disclose that zvegf3 is cleaved in vivo, and as Ferrara et al. state at column 4 that the protein may be obtained from human tissue, it stands to reason that protein so obtained would not comprise the CUB domain and would, when used as an antigen, result in precisely the antibodies claimed by the instant application.

Advisory Information:

The Claims merely recite "An antibody", and do not require any particular level of purity. Amendment of the claims to indicate that the claimed subject matter may not comprise antibodies to other portions of SEQ ID NO: 2, such as by adding the language "free from other antibodies" or a negative limitation restricting the claims from including such would remove the prior art rejections.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz,

at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector, Ph.D.
Primary Examiner

LMS
09/541752.2
3-10-03